

RECEPTOR BASED ANTAGONISTS AND  
METHODS OF MAKING AND USING

This application claims priority of International Application No. PCT US99/22045, filed on September 22, 1999 which claims  
5 priority of U.S. Application No. 09/513,942, filed May 19, 1999, which claims priority of U.S. Provisional Application No. 60/101,858 filed September 25, 1998. Throughout this application various publications are referenced. The disclosures of these publications in their  
10 entireties are hereby incorporated by reference into this application.

BACKGROUND OF THE INVENTION

Although discovered for varying biological activities, ciliary neurotrophic factor (CNTF), leukemia inhibitory factor (LIF), oncostatin M (OSM) and  
15 interleukin-6 (IL-6) comprise a defined family of cytokines (referred to herein as the "CNTF family" of cytokines). These cytokines are grouped together because of their distant structural similarities [Bazan, J. Neuron 7: 197-208 (1991); Rose and Bruce, Proc. Natl. Acad. Sci. USA 88: 8641-8645 (1991)], and, perhaps more importantly, because they share "B" signal-  
20 transducing receptor components [Baumann, et al., J. Biol. Chem. 265:19853-19862 (1993); Davis, et al., Science 260: 1805-1808 (1993); Gearing et al., Science 255:1434-1437 (1992); Ip et al., Cell 69: 1121-1132 (1992); Stahl, et al., J. Biol. Chem. 268: 7628-7631 (1993); Stahl and Yancopoulos, Cell 74: 587-590 (1993)]. Receptor activation by this family of cytokines results from  
25 either homo- or hetero-dimerization of these  $\beta$  components [Davis, et al., Science 260: 1805-1808 (1993); Murakami, et al., Science 260: 1808-1810 (1993); Stahl and Yancopoulos, Cell 74: 587-590 (1993)]. IL-6 receptor activation requires homodimerization of gp130 [Murakami, et al., Science 260: 1808-1810 (1993); Hibi, et al., Cell 63: 1149-1157 (1990)], a protein initially  
30 identified as the IL-6 signal transducer [Hibi, et al., Cell 63: 1149-1157 (1990)]. CNTF, LIF and OSM receptor activation results from heterodimerization between gp130 and a second gp130-related protein known as LIFR $\beta$  [Davis,